ABSENCE OF THE EPITHELIAL HYPOPHYSIS IN A FETAL DOGFISH ASSOCIATED WITH ABNORMALITIES OF THE HEAD AND OF PIGMENTATION

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The specimen herein described is an albino fetus of the spiny dogfish (*Squalus acanthias*) which presents malformations of the head including cyclopia and astomia. Associated with these is the very rare anomaly—absence of the epithelial hypophysis. It is well known that there are abnormalities of the pituitary in human anencephalic fetuses, but these involve absence of the neural lobe. Covell (1927), in making a quantitative study of such abnormal human fetuses, reviewed the literature and reported personal observations comprising in all nearly a hundred cases. He concluded that an hypophysis is always present, although the lobus nervosus is lacking in the majority of specimens. The pars anterior he found constitutes most of the gland volume and in some cases the total volume. He mentions no case of absence of the anterior lobe. The only instance hitherto described of spontaneously occurring absence of the anterior pituitary, in any animal, is the case reported by Evelyn Holt (1921) of absence of the pars buccalis in a 40-mm. pig.

The study of the present specimen of an elasmobranch fetus has been undertaken not only on account of its rarity but because of the evidence of interdependence in development of the separate lobes of the pituitary gland and the effect of absence of the oral components of the gland on pigmentation.

Material and Methods

The fetus was discovered among a great number of normal *Squalus* pups, at the David Richardson Laboratory, Bailey Island, Maine. Because its abnormalities escaped notice when it was removed from the uterus, normal littermates are not available for study as controls. Two normal pups, from other uteri, but of a comparable stage of development, were selected, instead, as controls. The three fetuses were fixed in 7 per cent formalin. The heads were subsequently imbedded in celloidin, cut serially in 35 μ sections and stained with haematoxylin and eosin.

Description

The specimen is silvery white with the exception of the tip of the dorsal fin and the tip of the tail where in each case a small area is deep grey, approaching in intensity the color of a normal pup. The otherwise translucent skin is faintly clouded with light grey over the dorsum of the body, suggesting that the albinism is not due to complete absence of pigmentation. Aside from this general albinism, the obvious external deviations from the normal are limited to the region rostral to the first gill slits; the rest of the body is of normal configuration. The eyes give the appearance of having been drawn from their usual lateral position ventrally and medially to the midline where they are fused into a single dumbbell-shaped eye with two discrete lenses. There are no external nares; only a midventral prominence indicates where the olfactory bulbs have coalesced. The mouth is represented by a dimple-like depression and a narrow fold formed by a shallow, rostrally directed invagination of the integument (Fig. 1). In addition to these abnormalities of the head, it is noted that the yolk sac is exceptionally large as compared to that of normal fetuses.

Examination of the sections reveals radical departures from the normal structure of the cartilaginous cranium, a description of which requires frequent reference to the normal processes of development in order to understand and interpret them correctly. The base of the elasmobranch chondrocranium normally develops from two pairs of cartilaginous bars. The posterior or parachordal cartilages constitute the caudal part of the basis cranii. In the anterior or prechordal region, the cranial floor develops from paired trabeculae cranii whose rostral ends fuse in the midline to form the interorbital plate and the more anterior rostral plate. Between the diverging posterior ends of the trabeculae and the anterior edge of the basal plate is a median space, the fenestra hypophyseos, through which the hypophysis and carotid arteries gain entrance to the cranial cavity. The original hypophyseal connection with the oral cavity is gradually obliterated by centripetal growth of these cartilages. In the present malformed cyclopean fetus the abnormalities of the chondrocranium itself are limited almost entirely to the prechordal region. Cyclopean teratogenesis is generally believed to occur very early in embryonic development of the eyes and is attributed to a local arrest of growth ventrally, with fusion of the elements of the primary optic vesicles and normal growth of dorsal parts. It is commonly thought that the cyclopean eye obstructs the path of forward growth of the cranial trabeculae—and this appears to have occurred in the present specimen. As one can observe in Figs. 7 and 8, there is an amorphous horizontal plate

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of cartilage which overlaps the back of the posterior edge of the eye and extends caudally to the level of the spiracle. Even though this cartilage does not unite with the basal plate at any point, it seems probable that it represents a fusion of the trabeculae in a somewhat abortive attempt to grow forward past the obstructing eye. This cartilage does not approach the basal plate caudally, as might be expected, because of the interposition of jaw elements. The primordium of the mandibular arch normally takes the form of an inverted *U* at each corner of the mouth. In this specimen the dorsal parts of the head have unfolded normally, carrying lateralward the pterygoquadrate limb of the *U*-shaped cartilages while at the same time arrest of growth in the midventral line has caused the mandibular limb (Meckel's cartilages) to be crowded against the median basihyoid plate. Subsequently there appears to have been more or less fusion of these cartilages such that, at the level of Fig. 9, they constitute a single plate of cartilage in which the pterygoquadrate components are represented most laterally, Meckel's cartilages next, and the basihyoid cartilage in the middle. The homologies ascribed to the abnormal cartilaginous elements seem justified because the conspicuous adductor mandibuli muscle complex which normally surrounds the angle of the jaw between pterygoquadrate and mandibular elements (Fig. 9-*a*) is oriented with respect to the abnormal fused mass of cartilage precisely as would be expected if the above explanation were correct (Fig. 9).

The brain is for the most part normal save for minor readjustments in relation to the misplaced olfactory bulbs and retinae. In the normal dogfish the floor of the diencephalon bulges ventrocaudally forming the infundibulum which consists of two hollow oval lobes—the inferior lobes. A long tongue of glandular tissue consisting of the pars distalis and pars medialis of the pituitary extends anteriorly from the pars intermedia and may be seen lying in the groove between the inferior lobes (Fig. 5-*a*). At the level of the emergence of the oculomotor nerves the inferior lobes of the infundibulum are normally continuous with a thin-walled vascular outgrowth, the saccus vasculosus (Fig. 6-*a*), which is connected posteroventrally with the glandular intermediate lobe. At this point, in the normal animal, nervous tissue from the thickened floor of the saccus vasculosus is commingled with

PLATE I

FIG. 1. Ventral view of the abnormal *Squalus acanthias* fetus (natural size). The yolk-sac has been removed.

FIG. 2. Ventral view of a normal dogfish fetus.

FIG. 3. Dorsal view of the abnormal albino dogfish fetus.

FIG. 4. Dorsal view of a normal dogfish fetus.

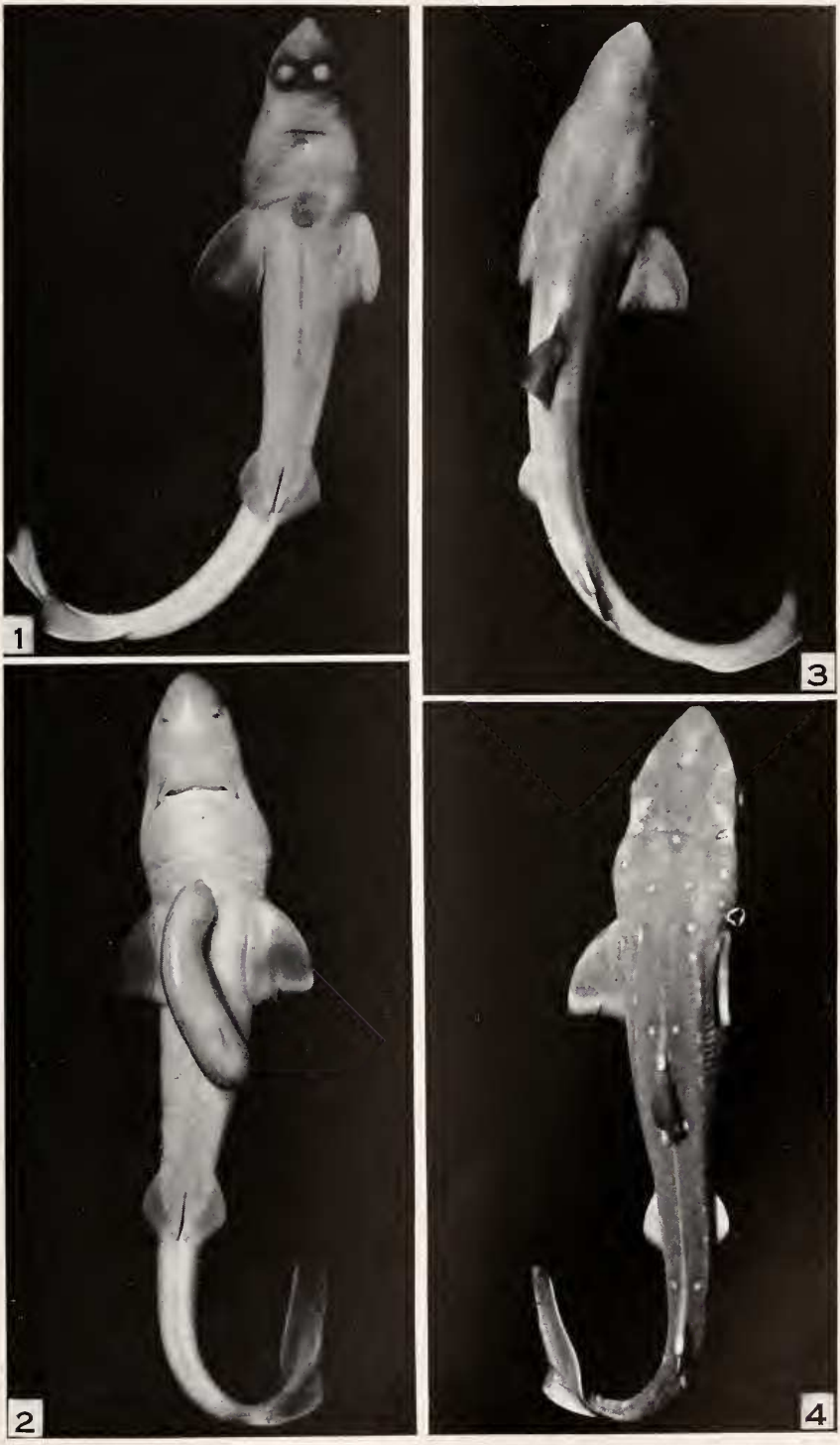

PLATE I

the glandular cords of the pars intermedia. The nervous tissue around this area of contact is usually thought to be the functional pars neuralis. The pars neuralis undergoes but little differentiation, the cells around

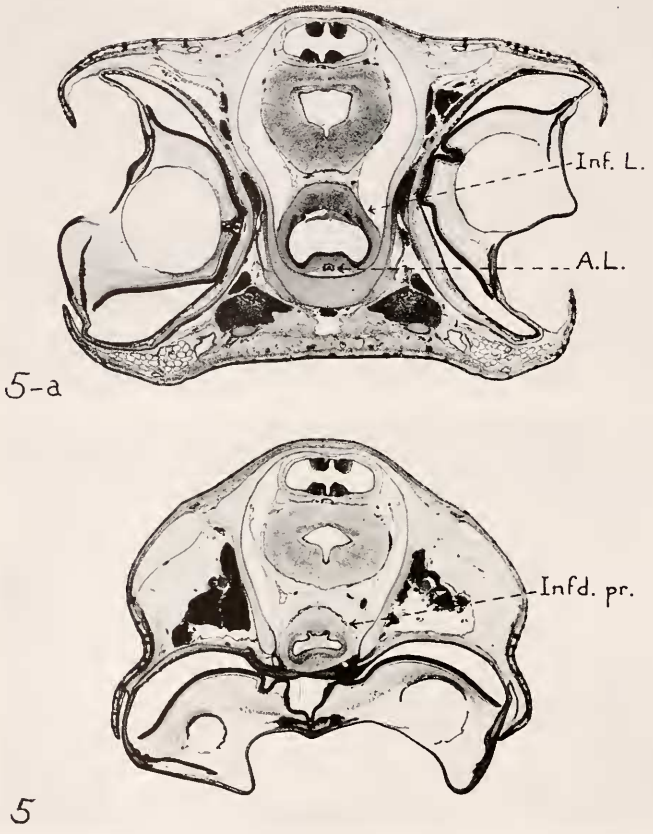

PLATE I

FIG. 5-*a*. A section of the head of a normal fetus showing the pars distalis of the anterior lobe (*A.L.*), lying in the groove between the inferior lobes of the infundibulum (*Inf.L.*). Photomicrograph (hematoxylin and eosin; × 4).

FIG. 5. A corresponding section of the head of the anomalous fetus showing no anterior lobe and a deformed infundibular process (*Infd. pr.*) not supported beneath by an interorbital plate of cartilage. Photomicrograph; × 4.

the infundibular lumen retaining much of the character of the embryonic ependymal layer (Butcher, 1936).

In the present abnormal specimen, on the contrary, the infundibulum extends posteriorly in a long conical process which, due to

absence of the anterior part of the cranial floor, is for some distance not supported beneath by cartilage but traverses the groove between the two dorsal convexities of the malformed eye (Fig. 5). This attenuated infundibulum becomes gradually more slender as it passes out of the cranial cavity beneath the anterior edge of the basal plate. The basal plate dorsally, the pterygoquadrate and mandibular rudiments laterally, and a ventral plate of cartilage (possibly the basihyoid) are all partially fused about a tubular space in which the narrow infundibulum is lodged (Fig. 7). Caudal to this point these fused cartilages separate from the base of the chondrocranium providing much more space for the infundibular process (Fig. 8). In consequence of this, the infundibulum expands at its caudal tip into a bulbous enlargement which ends blindly at the level of the spiracle in contact with the blind end of the entodermal pharynx (Fig. 9). The infundibular recess which extends from the third ventricle into the infundibular stalk is nearly obliterated at its narrowest point but finally terminates in a conspicuous cavity within the terminal bulbous enlargement of the neurohypophysis. At no place does the infundibular process show any tendency to differentiate into a saccus vasculosus.

The most striking abnormality of the pituitary is the total absence of the epithelial portions of the gland. No trace can be found of the parts of the pituitary deriving from the embryonic stomodeum—pars distalis, pars medialis, pars intermedia, and pars ventralis.

Discussion

The pigmentary deficiencies, the absence of all buccal components of the pituitary, and the aberrant infundibular process exhibited by this anomalous fetus are of interest in connection with the findings of P. E. Smith in albino tadpoles produced by early ablation of the pars buccalis of the hypophysis. It was shown by him that atypically placed buccal epithelium would induce hypertrophy of adjacent nervous tissue whereas in complete absence of the buccal hypophysis, the neural lobe did not attain its normal size, shape, or histological development. Evelyn Holt's 40-mm. pig, while lacking entirely the oral portion of the hypophysis, is described as possessing a pars neuralis "normal in position, extent, and structure." This, she points out, is contradictory to Smith's findings but it is noteworthy that her specimen is from a relatively early stage of development. If the pig fetus had had an opportunity to continue its intrauterine life, the further growth of the pars neuralis might well have been retarded or modified.

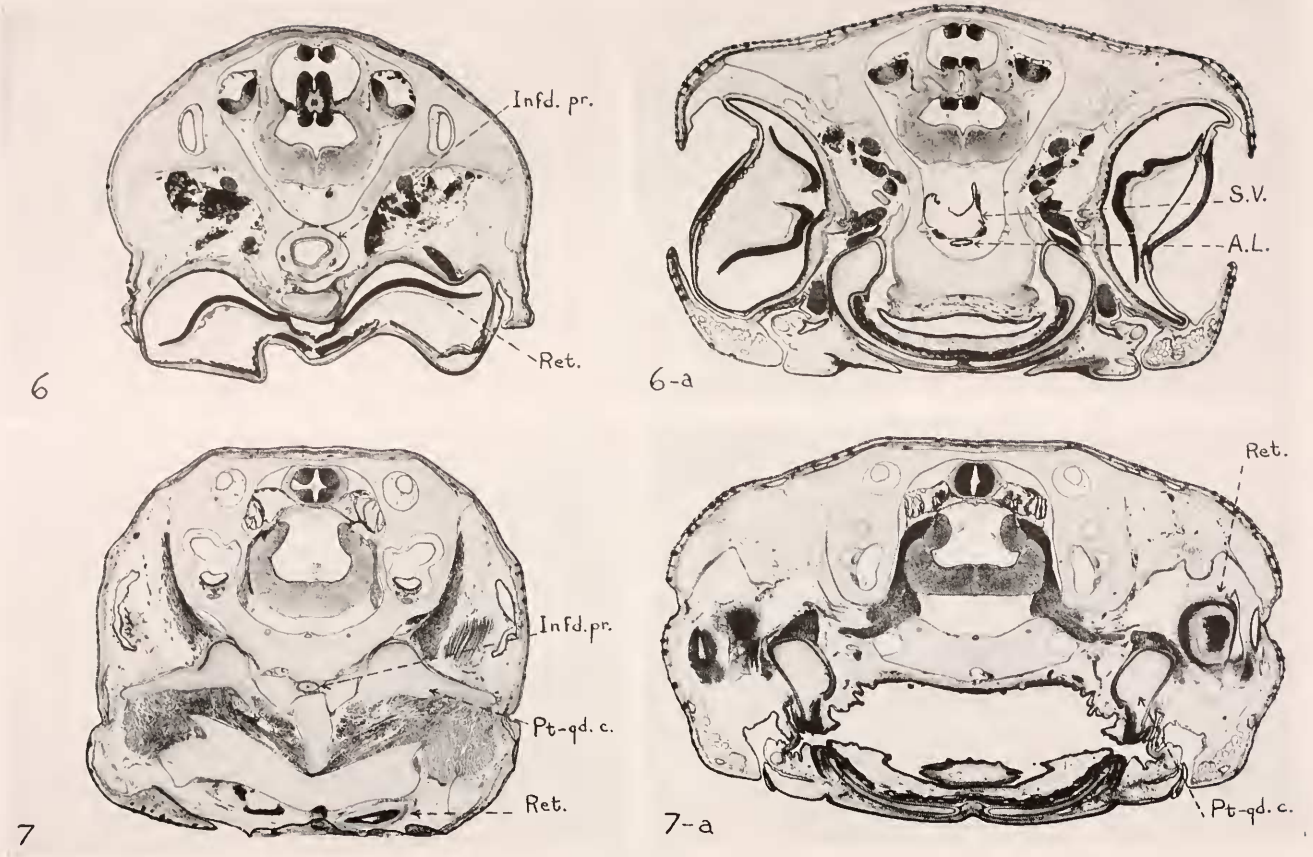

PLATE II

FIG. 6. Section of the head of the abnormal specimen showing the undifferentiated caudal extension of the infundibular process (*Infd. pr.*).

FIG. 6-*a*. Section at a corresponding level of the head of a normal control showing a saccus vasculosus (*S.V.*), and anterior lobe (*A.L.*) of the pituitary. Photomicrographs × 4.

FIG. 7. Photomicrograph of a section of the abnormal fetus at the level of the posterior edge of the retina (*Ret.*) showing the constricted region of the infundibular process (*Infd. pr.*) lodged between closely surrounding cartilages. Pterygoquadrate cartilage (*Pt-qd. c.*).

FIG. 7-*a*. Photomicrograph of a corresponding section of the normal control showing no part of the hypophysis present at

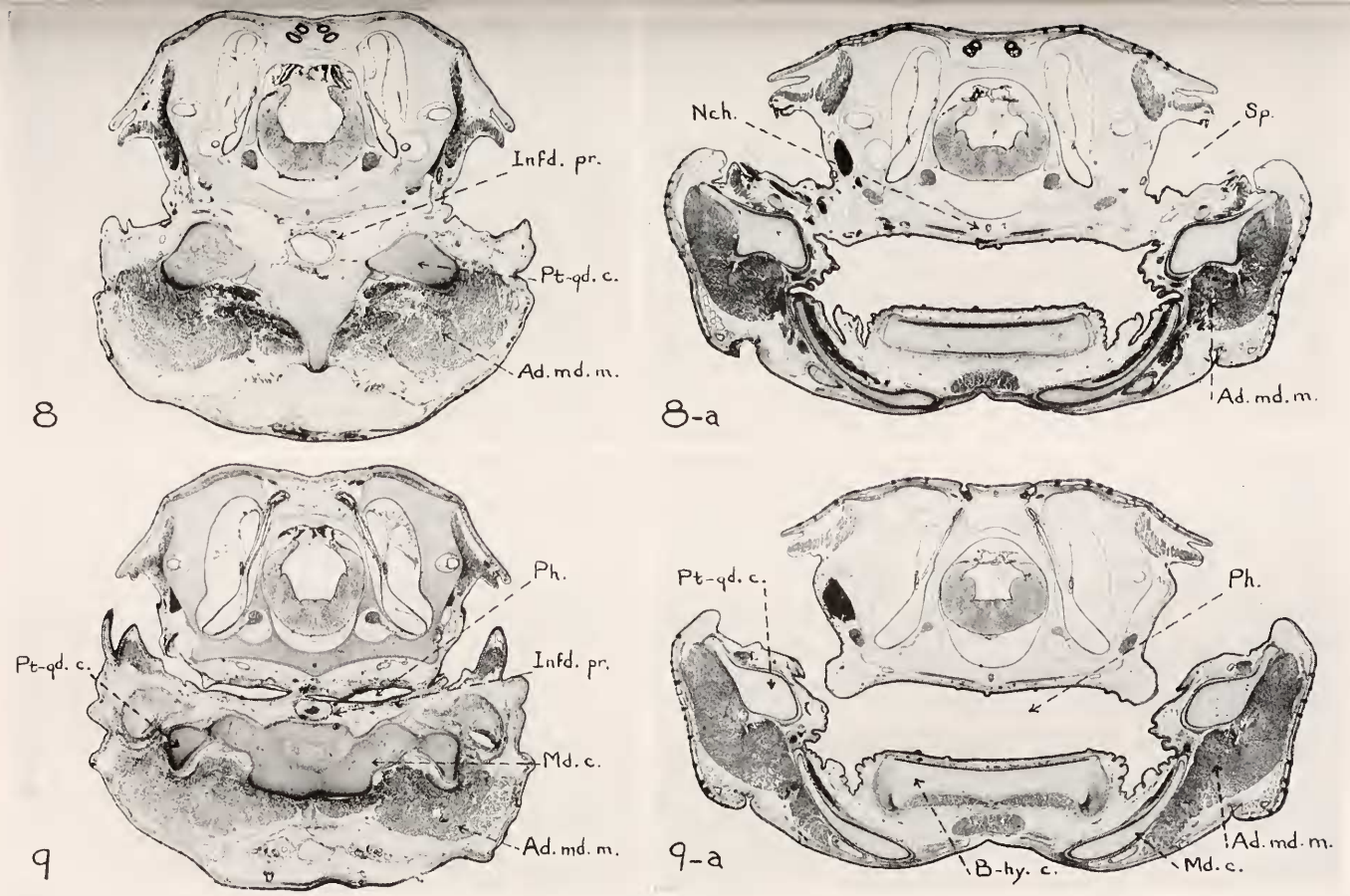

PLATE III

FIG. 8. Photomicrograph (× 4) of a section of the malformed specimen at the level of the spiracle (*Sp.*) showing the terminal bulbous enlargement of the infundibular process (*Infd. pr.*). The homologue of the pterygoquadrate cartilage (*Pt-qd. c.*) is associated with the conspicuous adductor mandibuli muscle (*Ad. md. m.*).

FIG. 8-*a*. A corresponding section of the normal control. At this level there is no part of the hypophysis.

FIG. 9. Photomicrograph of a section of the anomalous fetus at the level of the posterior edge of the spiracle showing the caudal end of the infundibular process in contact with the blind anterior end of the pharynx (*Ph.*). Mandibular cartilage (*Md. c.*).

FIG. 9-*a*. A corresponding section of a normal fetus. Pterygoquadrate cartilage (*Pt-qd. c.*). Mandibular cartilage (*Md. c.*). Basihyoid cartilage (*B-hy. c.*).

Furthermore, the interdependence in development of one part of the pituitary upon another may be quite different in mammals than in amphibia and fishes. The present case of pituitary agenesis in a lower vertebrate seems to bear out Smith's observations, for here, as in his tadpoles, in the total absence of the buccal ectoderm, the pars neuralis has not attained its normal shape nor has it undergone its typical differentiation into a saccus vasculosus.

Tadpoles in which the buccal hypophysis has been removed at an early stage of development display albinism in which the epidermal melanophores are diminished in number and pigment content besides remaining in a persistent state of contraction. These conditions in the tadpole are closely paralleled by this albino dogfish fetus in which the melanophores are less numerous, contracted, and noticeably withdrawn from the surface. Lundstrom and Bard, in a study of the effects of ablation of various parts of the brain of the dogfish (*Mustelis canis*), first discovered the hypophyseal control of the cutaneous pigmentation in the elasmobranch fishes. They found that removal of the neuro-intermediate lobe invariably resulted in pallor of the skin. The present anomalous specimen constitutes an interesting confirmation of their work. Evidently there has been a spontaneous suppression of the oral hypophysis equivalent to actual experimental ablation. Because of the intermingling of the elements of the pars neuralis and pars intermedia of the dogfish pituitary, it has so far been impossible to accomplish a complete operative separation of these two parts. The presence of the neuro-hypophysis in the present specimen, but the total absence of the oral pituitary (including the pars intermedia) indicates that the humoral agent affecting pigmentation is a derivative of the oral components of the gland. Presumably in that portion of the gland referred to as the neuro-intermediate lobe it is the buccal elements that are responsible for the chromatophore-expanding factor.

Observations in many cases of human anencephaly (Covell, 1927) make it apparent that aberrant formative processes involving defective closure in the dorsal midline may result in agenesis of the neural lobe of the pituitary. Cyclopia and astomia are occasionally found together in human monsters. It appears from the present observations that, in the dogfish, anomalous development in the ventral midline with imperfect separation of symmetrical parts and consequent cyclopia and astomia may result in agenesis of the oral hypophysis.

Summary

1. An anomalous fetus of the spiny dogfish (*Squalus acanthias*) is described in which there are malformations of the head comprising cyclopia, astomia, and abnormalities of the hypophysis.

2. The abnormalities of the hyophysis involve:—

(*a*) The total absence of the oral components of the gland, and

(*b*) A neural lobe which is deformed and possesses no saccus vasculosus. The conclusion is drawn that the neural lobe has not undergone normal differentiation because it has been deprived of its usual association with the buccal hypophysis.

3. The specimen is albino, displaying a diminished number of chromatophores in a state of persistent contraction. This finding indicates that the melanophore-controlling principle in the dogfish is a derivative of the buccal components of the pituitary.

4. Only one other instance of total spontaneous suppression of the oral hypophysis is described in the literature, namely, in a pig fetus (Holt, 1921). In human fetuses anencephaly occurs not infrequently but is associated with suppression of the neuro-hypophysis instead of with the adenohypophysis.

BIBLIOGRAPHY

Butcher, E. O., 1936. Histology of the pituitaries of several fish. *Bull. Mt. Desert Island Biol. Lab.*, pp. 18–20.

Covell, W. P., 1927. A quantitative study of the hypophysis of the human anencephalic fetus. *Am. Jour. Path.*, **3**: 17–28.

Holt, E., 1921. Absence of the pars buccalis of the hypophysis in a 40-mm. pig. *Anat. Rec.*, **22**: 207–216.

Lundstrom, H., and P. Bard, 1932. Hypophyseal control of cutaneous pigmentation in an elasmobranch fish. *Biol. Bull.*, **62**: 1–9.

Smith, P. E., 1920. The pigmentary, growth, and endocrine disturbances induced in the anuran tadpole by the early ablation of the pars buccalis of the hypophysis. *Am. Anat. Mem.*, No. 11, pp. 5–151.